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AN

EXPERIMENTAL ESSAY,

ON

THE MANNER IN WHICH OPIUM ACTS ON THE LIVING ANIMAL BODY.

BRITISH MUSEUM

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ON THE

LIVING ANIMAL BODY,

BY

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INTRODUCTION.

MANY of the firſt phyſiologiſts, both in Great Britain, and other countries, have endeavoured to aſcertain the manner, in which opium acts on the living animal body; and to their aſſiduity we are indebted for a vaſt number of experiments on this ſubject.

But the inferences, which one author makes from his obſervations, generally contradict thoſe of another; and the perplexity, ariſing from this ſource, is increaſed, by each having brought forward his own experiments and concluſions, without comparing them with thoſe, which had been made by others.

That I may avoid this error, I ſhall introduce the following paper, with a con ciſe view of the ſtate of our knowledge, concerning the action of opium on living animals, at the time my own experiments were begun. And, not to ſwell this part of the paper, by relating the arguments which each writer has uſed, in ſupport of his own hypotheſis, or againſt thoſe of others; or by giving any account of experiments, ſince proved inaccurate, I ſhall merely collect together the few ſeeming facts which remain, after rejecting the uſeleſs and inconſiſtent obſervations, in which they have been involved by the ingenuity of authors, and their partiality for particular opinions.

In various writers, we find the effects of a moderate doſe of opium, on living animals, accurately deſcribed; moſt people have experienced them, indeed, in their own perſons.

Soon after its exhibition, it renders the pulſe quicker and fuller, it produces relief from pain, and, in moſt inſtances, tranquillity of mind, and refreſhing ſleep.

The effects of opium, like thoſe of other drugs, become leſs conſiderable, the longer the body is accuſtomed to it. Every perſon knows, what quantities of opium are conſumed by the inhabitants of many eaſtern countries. And even in our own, we are every day meeting with people, who have habituated themſelves to a very free uſe of it. I have ſeen a man drink four ounces of laudanum, without perceiving from it even a tendency to ſleep.

Dr. Mead is among the earlieſt authors, who have given an accurate account of the effects of an over-doſe of opium.

In his Treatiſe on Poiſons, firſt publiſhed in 1702, he relates the following experiment made on a dog. "When he had thus "taken (ſays he), as I could gueſs, near "two drams of the ſolution, I watched "him about an hour; then he began to "ſleep, but preſently ſtarted up with con-"vulſions, fell into univerſal tremblings, "his head conſtantly twitched and ſha-"king; he breathed ſhort and with la-"bour, loſt entirely the uſe, firſt of his "hinder legs, then of his fore ones, which "were ſtiff and rigid like ſticks. As he lay "ſnorting, to haſten his end, I was giving

" him more of the ſolution, but, on a ſudden his limbs grew limber and he died."

Tralles, in his elaborate work, *De Uſu Opii*, gives nearly the ſame account of the effects of an over-doſe of opium. But, as he deſcribes theſe effects, ſuch as he accidentally met with them, in the human body, his account of them is more intereſting than that of moſt other authors. " Memini (he obſerves) horrendis convulſionibus affectum infantulum; cui, per errorem, datus fuerat pulvillus, matri deſtinatus, granulum forte dimidium, extracti opii, habens." He quotes ſeveral other ſimilar caſes from different authors.

The convulſions, produced by an over doſe of opium (it has ſince been obſerved), are of a peculiar kind. In many reſpects, they greatly reſemble tetanus. They are of that ſpecies, which has been termed tonic; have intermiſſions, and during theſe, are renewed by the ſlighteſt touch. I have repeatedly ſeen them excited by a perſon walking acroſs the room, while the animal lay on the floor; and have always obſerved the convulſions from an over-doſe of opium, in frogs and rabbits (the only animals on whom I have made the experiment), aſſume the form of a true opiſthotonos, without having ever perceived in them the leaſt tendency to any other form of tetanus.

Dr. Alſton, by means of the microſcope, obſerved the velocity of the circulation ſuddenly diminiſhed, on throwing a watery ſolution of opium into the ſtomach of a frog: But he has not ſtated

ted accurately, the time required for producing this effect.

He has alſo obſerved, that certain effects of opium, if it be given in large doſes, very ſuddenly follow its exhibition. It has almoſt inſtantly produced ſleep, relief from pain, from teneſmus, from vomiting, &c. From ſuch obſervations, Dr. Alſton draws a very fair concluſion, that opium is capable of acting on the ſyſtem in general, through the medium of the nerves, to which it is directly applied,

He has likewiſe ſhown, that a ſolution of opium, injected into a vein, produces the ſame effects, as when received into the ſtomach. In ſmall quantity, it occaſions no remarkable ſymptom; injected more freely, convulſions and death. It has been farther obſerved by various authors, that opium, applied to the brain, or injected into the heart and blood veſſels, produces convulſions more ſpeedily, than when exhibited in any other way.

Dr. Alſton found that opium thickens the blood, when mixed with it out of the body. It was a ſimilar obſervation, which gave riſe to the hypotheſis of its occaſioning death, by congealing the blood in the heart and large veſſels. His paper on opium is in the 5th volume of the Edinburgh Medical Eſſays and Obſervations.

Such was nearly the ſum of our knowledge, concerning the action of opium on the living animal body, when Dr. Whytt publiſhed his treatiſe on this ſubject.

In ſtating the additional information which he gives us, I ſhall paſs over, in ſilence, certain concluſions, which, it may ſeem at firſt ſight, I ought to have mentioned. On comparing them with the obſervations of later writers, however, they will be found inaccurate. His concluſions, for inſtance, concerning the manner, in which opium, applied to a diſtant part of the body, affects the motion of the heart.

Theſe are more generally known, and have been more frequently referred to, than perhaps any other part of his treatiſe, notwithſtanding they were, in a great meaſure, invalidated by the obſervations of Dr. Monro, as early as 1761; and have ſince been completely refuted, by a very accurate experiment of Fontana's, made on a large ſcale. As this experiment is related in the Appendix to his work on Poiſons, and conſequently not referred to in the General Index, it has often been overlooked. In a treatiſe lately publiſhed, on the influence diſcovered by Galvani, the author, in one part of his work, builds much of his reaſoning on the concluſions of Dr. Whytt, which are here alluded to.

Dr. Whytt, as well as Haller, found the motion of the heart little affected, by the application of a watery ſolution of opium to its external ſurface. But the former ſhewed, contrary to an opinion which once prevailed, that the heart is far from being wholly exempted from the action of opium: And, what may ſeem curious, he found, that a ſolution of this drug, thrown into the ſtomach and inteſtines of a frog, affects its motion more ſpeedily than decollation, and the deſtruction of the ſpinal marrow; and, on the other hand, that a large doſe of opium deſtroys the voluntary motions of this animal, in a ſhorter time than cutting out the heart.

Dr. Whytt farther obſerved, that opium, thrown into the ſtomach and inteſtines of a frog, or merely applied to its abdominal muſcles, produces effects leſs powerful and ſudden, than when injected into the cavity of the abdomen.

Upon the whole (he remarks), opium produces all its effects moſt ſpeedily on thoſe animals, which cannot live long without a freſh ſupply of food and air.

By many of the experiments juſt alluded to, as well as by others, he confirms

Dr. Alſton's opinion, that opium produces many of its effects, through the medium of the nerves, to which it is directly applied. To this action of opium probably is to be attributed the following fact, the laſt I ſhall mention, from Dr. Whytt's treatiſe, namely that opium, injected into the great guts of a dog, affects the hinder extremities, more ſpeedily than the fore ones,

I cannot, however, conclude my obſervations, on what this ſubject derived from the labours of Dr. Whytt, without quoting from his paper the following paſſage, which, as far as I can judge, either from my own experiments, or from thoſe of others, contains one of the juſteſt, and, at the ſame time, one of the moſt important obſervations, concerning the action

tion of opium on living animals, I have any where met with.

“ It remains (ſays he), therefore, that
“ opium, by affecting the extremities of
“ the nerves of the part to which it is ap-
“ plied, does, by means of their connection
“ and ſympathy with the brain and ſpinal
“ marrow, deſtroy or prevent, through the
“ whole nervous ſyſtem, the operation of
“ that power, upon which depends ſenſa-
“ tion and motion in the bodies of ani-
“ mals.” It is to be remarked, that Dr. Whytt does not here ſpeak of the ſympathy of nerves, but of their connection with the brain and ſpinal marrow.

Not long after the publication of Dr. Whytt's treatiſe, Dr. Monro publiſhed his obſervations on the ſame ſubject, in the 3d volume of the Eſſays and Obſervations, Phyſical and Literary, of the Philoſophical Society of Edinburgh.

Dr. Monro ſhews, that opium, applied externally, produces the ſame effects, as when thrown into the ſtomach and inteſtines, cavity of the abdomen, or blood veſſels. He obſerves, page 306, "The ef-
" fects are, however, more ſpeedy, where
" the doſe is equal, when the opium is
" applied inwardly, than when applied
" outwardly; as might have been preſu-
" med, from the greater ſenſibility and
" delicacy of the inward organs."

He has alſo ſhewn, that, although opium, applied to a naked muſcle, very ſuddenly deſtroys its power of contraction, yet, applied externally to a limb, while the ſkin is entire, it does not affect its muſcles more ſpeedily, or in a greater degree, than the muſcles of any other part of the body.

Having obſerved the effects of opium on the entire animal, he wiſhed to aſcertain its effects, when it acts merely on the part to which it is directly applied.

" But here (he obſerves), we per-
" ceive an obvious difficulty; for, if
" we ſtop the circulation in every part
" of the body, by cutting out the heart,
" or ſtop it in one particular part; it is
" evident, that the animal will be dead,
" or the nerves will have loſt their ener-
" gy, in a great meaſure, if not entirely,
" before the ſolution of opium can pro-
" duce its effects in a very obſervable
" manner."

This difficulty, however, was obviated in the following manner: Dr. Monro found, analogous to an obſervation of Dr. Alſton, that, on pouring 30 drops of a ſtrong ſolution of opium, through a hole made in the abdomen of a frog, the motion of the heart is ſo ſuddenly affected, that, in the ſpace of two minutes, it beats with only half its uſual frequency, and that, ſoon afterwards, all the muſcles of voluntary motion are convulſed.

"Having, by this laſt experiment (he "obſerves), diſcovered a method by which "this animal (the frog) is affected to a "violent degree with opium, in a ſhorter "time, than that in which the energy of "its nerves is conſiderably impaired, by "putting a ſtop to the circulation; I could "now determine, with certainty, whether "this animal could be affected in that violent degree, through the nerves to which

" the opium was primarily applied, independent of abſorption, and the circu" lation of the blood, by cutting out the " ventricle of the heart, and ſo ſtopping " the circulation, before I poured the " ſolution into the cavity of the abdo" men; and on ſeveral trials, I found, " that the animal was in this way affect" ed as in the laſt experiment," (*i. e.* the animal was convulſed); " with this only " difference, that it required a ſomewhat " longer time to produce theſe effects in " the ſame degree.

The author, in his comment on this experiment, obſerves, " As the animal " was convulſed, and in a ſhort time kill" ed, by pouring the ſolution into the " cavity of the abdomen, after cutting " out the heart, we have undeniable evi" dence, that there is a poſſible way of

" applying opium, ſo that it may produce " thoſe effects, through the nerves, to " which it is primarily applied, independent of its abſorption and circulation " with the blood, as Dr. Whytt, from a " ſimilar experiment, firſt endeavoured to " prove."

Dr. Monro has alſo ſhewn, that the ſame effects are produced by throwing the ſolution of opium into the heart, while the heart itſelf is inſtantly rendered paralytic.

" When we compare that part of the " foregoing experiment which relates to " the heart, (ſays the author), with ſome " experiments made by Dr. Whytt, " where the opium was applied to its " outer part, we ſee how greatly the delicacy of feeling of the inner ſide of

" the heart exceeds that of the outer " ſide." And in another place he obſerves, " We ſee how ſuddenly the whole " body ſympathiſes with the heart."

On looking over notes which I took from his lectures in 1789, I find it mentioned, that although the aorta be previouſly cut, a ſolution of opium thrown into the heart affects every part of the body. And in a late paper, entitled, *Experiments on the Nervous Syſtem with Opium and Metalline Subſtances, made chiefly with the view of determining the Nature and Effects of Animal Electricity*, he obſerves, " Many years ago, I found, after cutting " the venæ cavæ and aorta of a frog, that " a watery ſolution of opium, poured into " the heart, occaſioned in a few minutes " convulſions in its legs; and after cutting

" out the heart, that the opium poured
" into the cavity of the abdomen affected
" the legs in like manner; although, in
" theſe experiments, the circulation was
" not only interrupted, but the greater
" part of the blood evacuated. I there-
" fore then concluded, and now conclude,
" that opium and other poiſons, even af-
" ter they are mixed with the maſs of
" blood, produce their fatal effects chiefly,
" and almoſt ſolely, by acting on the
" nerves of the heart and vaſcular ſyſtem."

Yet Dr. Monro found, that opium, applied to the extremities, is not capable of affecting the whole ſyſtem through the medium of the nerves.

But the moſt important point concerning the action of opium on living animals, eſtabliſhed by this author, is its being received into the ſyſtem by means of the abſorbents: which, as far as I can judge, he proves inconteſtibly, by ſhewing that the effects of opium, applied to a limb, after all communication between it and the reſt of the body, by means of the nerves, is cut off, are ſoon felt in every part of the ſyſtem.

Such are the circumſtances relating to the action of opium on the living animal body, aſcertained by Dr. Monro. The following concluſions, which I ſhall give in his own words, contain the leading opinions he formed on this ſubject.

" We may indeed perceive, (ſays he), " that the effects of all the foregoing me- " dicines, (among which opium is inclu- " ded), when they are applied to the " ſound outer ſurface of the body, are

" chiefly owing to their abſorption, mix-
" ture, and conveyance with the blood;
" ſince they operate as violently, and
" nearly as ſoon, when the nerves of the
" part to which they are applied are cut,
" as when they are entire.

" If, again, they are applied to the
" more ſenſible inward ſurface of the
" primæ viæ, they may probably operate
" more ſpeedily, and in ſome caſes more
" violently, through the nerves alone,
" than by their being abſorbed, and con-
" veyed by the blood."

In another place he obſerves, " As the
" opium has a ſurpriſing influence over
" the heart and arterious ſyſtem, when
" directly applied to them, and theſe ef-
" fects, though greater, are ſimilar to the
" effects of this medicine when abſorbed,
" we

" we may infer, that when it is abſorb-" ed, mixed, and conveyed with the " blood, its effects are almoſt ſolely to be " aſcribed to its operation on the nerves " of the heart, and veſſels through which " it is carried; and, by analogy, the " like is probable of many other medi-" cines."

In his 12th corollary, he remarks, " We are to conſider, that the nerves of " the heart, and large branches of the " vaſcular ſyſtem, affected by medicines " abſorbed and conveyed by the blood, " will influence by ſympathy other nerves " of the body, to which theſe medicines " may not be able to penetrate through " the very ſmall veſſels."

" But (he obſerves in another of his " corollaries) it is difficult to determine

" whether we are to aſcribe the chief ef-
" fects of opium on the ſound animal to its
" action on the nerves, to which it is im-
" mediately applied, or to its abſorption."

I ſhall quote but one more obſervation from Dr. Monro's paper. It deſerves particular attention. That part of it which relates to opium, indeed, is ſuggeſted by what has already been ſaid, namely, "That the effects of an over-doſe of
" opium, as well as of ſome other medi-
" cines, on frogs, are analogous to their
" effects on men and quadrupedes."

Fontana, the well-known Italian phyſiologiſt, makes a ſimilar remark. This author, among numerous experiments relating to other ſubjects, has made many with opium on living animals.

Only a ſmall part of what he has done on this ſubject, however, falls to be taken notice of here. He does not ſeem well acquainted with what had been aſcertained by the phyſiologiſts of this country, before he publiſhed his experiments; and frequently beſtows much pains endeavouring to prove, what has already been ſtated, as proved by others.

His experiments, indeed, ſeem accurate, and many of them are made on a ſcale even more extenſive than was neceſſary for aſcertaining what he had in view; but he draws few concluſions; and the imperfect manner in which moſt of the experiments are related ſeldom admits of any, but thoſe which the author makes from them.

This doubtleſs proceeded from his having in view to prove but one great fact, and neglecting (as every perſon in ſuch circumſtances is more or leſs apt to do) whatever did not tend to ſupport or overthrow his favourite hypotheſis. A few of his experiments deſerve particular attention.

By one, made on no leſs than 300 frogs, he has aſcertained, that opium applied to a nerve does not affect the muſcles in which it terminates.

It is foreign to the plan which, for the ſake of brevity, I have adopted, to comment upon the inference that Fontana draws from this experiment, "Que le "vehicule de l'opium eſt la circulation "du ſang et des humeurs dans l'animal: "et que ſans elle l'opium n'exerceroit "aucune action ſur corps vivant." It is directly contradicted by almoſt innumerable obſervations,

The following experiment of Fontana's is one of more conſequence. It was alluded to when ſpeaking of Dr. Whytt's treatiſe on opium. An experiment of this author ſuggeſted it to Fontana. "I made (ſays the latter) a little opening in the ſcull of a certain number of frogs, through which I deſtroyed the brain and ſpinal marrow with a long pin. By performing the experiment in this way, rather than by cutting off the head, the great flow of blood which takes place in decollation was prevented; and conſequently, in making experiments, frogs, with the nervous ſyſtem deſtroyed in this way, can be more readily compared with the entire animal. Having then (he continues) made a certain number of frogs, thus prepared, ſwallow each a certain quantity of opium, and the ſame number of entire frogs ſwallow each the ſame quantity, I opened the thorax in all of them, in order to obſerve the motion of the heart. I obſerved its duration, and from time to time ſtimulated the crural nerves, both in the one ſet of frogs and in the other; and I can aſſert, that having uſed in this experiment 48 frogs, 24 with the brain and ſpinal marrow, deſtroyed as above mentioned, and 24 entire, I could not perceive, that the opium produced a leſs effect, or operated more ſlowly, on the one ſet of frogs than it did on the other.

" Je deduis cependant, de ces reſul-
" tats, (Fontana continues), deux corol-
" lairs tres importans : Le premier eſt,
" que le mouvement du coeur ne depend
" point

“ point des nerfs, ni de cet enſemble de
“ ſenſations qui conſtitue la vie de l'ani-
“ mal. Le ſecond eſt, que l' action de
“ l' opium l' exerce independamment du
“ ſyſteme nerveux.”

The former of theſe inferences is made from other experiments. It is plain, that the latter is not warranted by that juſt related. The only concluſion we can draw from it, and one indeed which it is impoſſible for us not to draw from it, is, that the motion of the heart is not affected by opium, applied to a diſtant part of the body, through the medium of the nervous ſyſtem.

It is eaſy to count the beats of the heart, but impoſſible to determine accurately the ſtate of the muſcles, by irritating the nerves which terminate in them.

This part of the experiment lies open to much fallacy; and that Fontana was deceived in the inference which he draws from it, appears from many facts related in the ſubſequent part of this paper.

Fontana found, in another experiment made on 24 frogs, that opium, thrown into the ſtomach, more ſpeedily impairs the motion of the limbs in the entire animal, than in one with the heart cut out.

Dr. Alexander publiſhed his theſis, entitled, " De partibus corporis animalis " quæ viribus opii parent," at Edinburgh, in 1790. He attempts to ſhow, (contrary to what ſeems aſcertained by ſeveral of Dr. Monro's experiments), that opium is never received into the ſyſtem by means of the abſorbents.

I think it neceſſary to mention this attempt, becauſe Dr. Alexander's experiments have been made ſince the publication of Dr. Monro's. But how unſucceſsful it is, muſt appear at firſt view to every perſon who peruſes the theſis.

No body can compare together the 52d, 54th, and 56th experiments, and read the comment which in the 106th and 107th pages the author makes upon them, without ſome ſurpriſe at ſeeing a man of Dr. Alexander's ingenuity permit himſelf to be ſo evidently miſled.

Can it be ſeriouſly aſſerted, that becauſe a frog with the ſpinal marrow divided, and 30 drops of a ſolution of opium applied to the extremities, ſurvived another whoſe heart was cut out, and to whoſe extremities the ſame quantity of the ſame ſolution was applied: Can it be aſſerted, I ſay, from this experiment, that none of the effects of opium depend upon its abſorption? Is not cutting out the heart more ſuddenly fatal than the diviſion of the ſpinal marrow? and ſhall we make no allowance for this circumſtance in drawing our concluſions from the experiment?

Nor are his 59th and 60th experiments concluſive *, ſince opium, applied to the inferior extremities, operates very ſlowly on

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* Neither is Dr. Alexander's 51ſt experiment concluſive. The powers of abſorption were probably deranged by the injury done to the part of the inteſtines on which the experiment was made. Beſides, it was no eaſy matter to determine whether or not the lacteals contained a ſmall quantity of the

on the ſyſtem in general; and the injury done to the frogs in theſe experiments, previous to the application of the opium, was very conſiderable *.

From ſome of Dr. Alexander's experiments it appears, that univerſal convulſions are the conſequence of throwing a ſolution of opium into the ſtomach and inteſtines of a frog, although the heart has been previouſly removed. It was formerly obſerved, that Dr. Monro met with the ſame reſult, on injecting a ſolution of opium into the cavity of the abdomen, after cutting out the heart; but he ſpeaks as if he did not meet with this

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* Dr. Alexander was led, from his experiments on this head, to conclude, upon the whole, that although we cannot poſitively aſſert that opium is not abſorbed, yet we have no proof of its being ſo, at leaſt to ſuch a degree as to kill.

reſult when the ſolution was thrown into the ſtomach and inteſtines.

Dr. Alexander ſhews, by many experiments, that opium, injected into the heart of a frog; or into the ſtomach and inteſtines, or under the ſkin, whether the heart has been previouſly removed or not; deſtroys the irritability of all the muſcles of voluntary motion: but that it only produces the ſame effect on the muſcles of involuntary motion when immediately applied to them.

He has alſo ſhewn, that if the nerves going to any limb be cut, the irritability of that limb remains after death, when the animal is killed by opium, in whatever manner applied, provided it has not been applied to the muſcles of the limb itſelf.

As moſt of Dr. Alexander's experiments were made with a view to ſupport or overturn certain hypothetical opinions, and as no inferences of conſequence, except thoſe relating to ſuch opinions, can be drawn from them, few of this author's uſeful obſervations fall to be related here.

The laſt fact mentioned from Dr. Alexander's treatiſe is farther confirmed by Dr. Fowler, in a publication above alluded to, who uſed, as a teſt of the irritability of the muſcles, the influence lately diſcovered by Galvani.

It may not be uſeleſs to preſent, at one view, the moſt important facts which have been ſtated.

Opium, applied to any part of a living animal, ſoon produces an averſion to motion, and a tendency to ſleep. Theſe effects often take place inſtantly when the doſe is conſiderable, eſpecially if it has been applied to a ſenſible part of the body *.

If the doſe is ſufficient to endanger life, convulſions ſoon ſucceed, which conſiſt of repeated contractions and relaxations of all the muſcles of voluntary motion †. In different caſes the contractions are more or leſs permanent.

Throwing a ſolution of opium into the blood-veſſels produces the ſame effects as applying it in any other manner. A ſmall quantity may be given in this, as in every other way, without occaſioning either

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* Dr. Mead.

† Dr. Mead, Dr. Alſton, Dr. Tralles, &c.

either convulſions or death [*]. Convulſions are the conſequence of throwing a ſtrong ſolution of opium into the heart of a frog, whether the venæ cavæ and aorta have been previouſly divided or not [†]. The ſame ſolution thrown into the ſtomach and inteſtines, or into the cavity of the abdomen, after the heart is cut out, produces the ſame effect [‡].

After the brain and ſpinal marrow of a frog have been deſtroyed, without much loſs of blood, a ſolution of opium, thrown into the ſtomach and inteſtines, affects the motion of the heart as readily as when the nervous ſyſtem remains entire [‖]. Opium, therefore, applied to a

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[*] Dr. Alſton, Fontana, and Dr. Alexander.

[†] Dr. Monro.

[‡] Dr. Monro and Dr. Alexander.

[‖] Fontana.

diſtant part, affects the motion of this organ through ſome other medium than that of the nervous ſyſtem.

After all connection, by means of the nerves, between the hinder-limbs and trunk of a frog, is cut off, a ſolution of opium applied to theſe limbs produces the ſame effects on the body in general, as when their connection with the trunk is entire. From which we conclude, that opium is received into the ſyſtem by means of the abſorbents *.

On throwing a ſtrong ſolution of opium into the heart, it inſtantly becomes paralytic; nor can its action be renewed by any irritation whatever *.

The

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* Dr. Monro.

The application of this ſolution to the muſcles of the extremities produces the ſame effect on them. But if every thing forming the connection between theſe and the trunk, except the nerves, be divided, its action extends no farther *.

Thrown into the heart of a frog; or into the ſtomach and inteſtines, or under the ſkin, either before or after the heart is removed; it deſtroys the irritability of all the muſcles of voluntary motion †.

Thrown into the cavity of the abdomen, it very ſuddenly renders the contractions of the heart leſs frequent ‡, and produces all its other effects more ſpeedily than when injected into the ſto-

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* Dr. Monro.

† Dr. Alexander.

‡ Dr. Monro.

mach and inteſtines, or merely applied to the abdominal muſcles *.

Laſtly, it operates moſt ſpeedily on thoſe animals which cannot live long without a freſh ſupply of food and air †.

Such may be conſidered the preſent ſtate of our knowledge concerning the action of opium on the living animal body.

On reviewing what has been ſaid, we ſtill find the ſubject involved in much confuſion.

Opium, it has been obſerved, ſo affects the nerves of the abdomen, ſtomach, and inteſtines,

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[*] Dr. Whytt and Dr. Monro.

[†] Dr. Whytt.

inteſtines, and thoſe of the heart, as to act by what has been termed the Sympathy of Nerves, on every, the moſt diſtant part of the body, after the circulation is interrupted; and yet no action of opium on the nerves of the extremities produces the ſame effect. And altho' a ſolution of opium, directly applied to the heart, thus affects diſtant parts of the body, and the motion of this organ is almoſt immediately influenced by injecting the ſolution into the cavity of the abdomen, *i. e.* far more ſpeedily than it could be through the medium of the abſorbents; yet throwing a large quantity of opium, into the ſtomach and inteſtines, does not affect the motion of the heart, through the medium of the nervous ſyſtem.

Theſe circumſtances very nearly imply contradictions, and certainly do not tend to eſtabliſh any general laws concerning the action of opium on living animals.

My reaſon for laying the following experiments before the public is, that they contradict many of the moſt eſſential of the above-mentioned circumſtances, at preſent regarded as inconteſtible facts; that they remove the ſeeming contradictions juſt ſtated; and that they ſeem to afford a very ſimple account of the modus operandi of opium on living animals; that is, to ſhew on what parts of the ſyſtem this drug immediately acts in producing each of its effects, and that its action on theſe parts does not eſſentially differ from that of a vaſt number of other ſubſtances.

But I do not aſſert, that becauſe they

remove theſe ſeeming contradictions, and afford a more ſimple account of the modus operandi of opium than thoſe which have been related or alluded to; I am very far (I ſay) from aſſerting, that on theſe accounts their reſults ought to be granted; eſpecially when they contradict the inferences which we muſt draw from the experiments of a Whytt, a Monro, or a Fontana.

The only means of arriving at certainty in experiments, where there is ſo much room for fallacy as in thoſe I am ſpeaking of, is frequently repeating them; and although the circumſtances juſt mentioned tend doubtleſs to confirm the reſults of the following experiments, it is ſolely on this ground that I bring them forward, namely, that they have been much more frequently repeated than thoſe, from which oppoſite concluſions muſt be drawn.

EXPE-

EXPERIMENTS, made with a view to determine the manner in which Opium acts on the Living Animal Body.

I Begun theſe Experiments by repeating the moſt ſimple of thoſe which had been made by others. Opium was applied to various parts of the entire animal, both external and internal, and the reſults found preciſely ſuch as various authors have ſtated them.

The animal conſtantly became affected

with violent and univerſal ſpaſms, which almoſt immediately followed the exhibition of the opium, when it was applied to the brain, or injected into the heart and blood-veſſels.

After making many experiments which led to no uſeful concluſion, any account of which, therefore, would be improper, the following obſervation ſuggeſted ſeveral of thoſe, I am about to relate.

On throwing a ſolution of opium into the heart, I thought I perceived it paſs along the aorta towards the brain. Comparing this circumſtance with the effects of opium applied to that organ, it appeared probable, that the convulſions which follow its injection into the heart and blood-veſſels, are owing, not to any ſympathy of the nerves of the heart with thoſe of other parts of the body, but to the opium being conveyed through the aorta, and immediately applied to the brain. With a view to determine this point, I made the following experiments.

The ſolution uſed in the firſt and many of the other experiments, was prepared in the following manner. One ounce of opium was triturated with two ounces of warm water, till a turbid mixture was formed: one ounce of cold water was afterwards added to it. This mixture was carefully corked, and expoſed to a temperature of 90° * for 12 days. It was then

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* Of Farenheit's thermometer.

then filtered, and about two ounces and a half of a very ſtrong ſolution obtained, which appeared almoſt black in a common two-ounce vial. This ſolution is ſtronger than that which was uſed either by Dr. Monro or Dr. Alexander. A weaker was prepared by mixing equal parts of this ſolution and water *.

After ſecuring the aorta by ligature in 12 frogs of different ſizes, a few drops of the ſtrong ſolution of opium was injected into the heart of each. It immediately ceaſed moving. This, however, was not followed by the ſlighteſt convulſion in any part of the body.

The

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* In many of the following experiments, it is of no conſequence to know the ſtrength of the ſolution employed: it is not therefore attended to in theſe.

The frogs all died in exactly the ſame manner as theſe animals do when the heart is cut out; that is, when the circulation is interrupted, and when they loſe as much blood as in this experiment. I could not perceive that the injection of the ſolution had any effect, but that of putting a ſtop to the motion of the heart.

The irritability of the muſcles of voluntary motion, after death, was found, in all of theſe frogs, as entire as it is after any death equally lingering.

A ſimilar experiment was made in the following manner: After dividing the aorta in ten frogs, moſt of them full grown, a few drops of a ſolution of opium, (not quite ſo ſtrong as that uſed in the laſt experiment), were thrown into the heart of each. Its contractions inſtantly ceaſed, but no convulſions ſupervened.

I have neglected, I find, to mention in my notes the degree of irritability remaining, after death, in the muſcles of theſe frogs. I ſeldom or never failed to examine it, however, and I recollect, that in all experiments of this kind, that is, in which a ſolution of opium was injected into the heart, after dividing the aorta, or ſecuring it by ligature, the muſcles of voluntary motion were readily thrown into contractions, after death, by irritating the nerves which terminate in them.

A circumſtance which occurred in making this experiment, ſerves, in ſome meaſure, to account for others having met with a different reſult from it. Having divided the aorta, as I imagined, and injected ſome drops of the ſolution into the heart of a frog, I was ſurpriſed to obſerve, (contrary to what happened in the experiment juſt related), the animal ſeized with univerſal convulſions.

On examining the part of the aorta, however, at which the cut had been made, the cauſe of this difference of reſult appeared very evident. I had not completely divided the artery, the two ends ſtill adhered by a ſlight connection on the inner ſide of the veſſel; and as the elaſticity of its ſides preſerved its cavity, any fluid injected into the heart muſt in part have paſſed along this veſſel to the brain. The conſequence would have been the ſame, it is evident, had the cut ends of the veſſel been kept applied, or nearly ſo, by cellular membrane, or any other means.

I accidentally obſerved, in more than one inſtance, that convulſions did not ſupervene, when the ſolution was injected into the heart in very ſmall quantity, and with very little force, although the aorta was neither divided nor ſecured by ligature. This mode of making the experiment is certainly more concluſive than either of the foregoing; ſince many of the nerves of the heart paſs ſo near the aorta, that they muſt ſhare its fate, when we divide or throw a ligature around this veſſel.

But it is almoſt impoſſible to repeat the experiment frequently in this way with the ſame reſult. It is difficult to inject the ſolution in ſuch a manner, that no part of it may paſs into the aorta, or always to determine whether it does ſo or not *.

This, however, ſuggeſted another mode of making the experiment, which ſeems perfectly concluſive.

I ſlit the heart in ſix frogs. Notwithſtanding its contents were thus inſtantly evacuated,

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* This mode of making the experiment, although its reſult is not always uniform, ought perhaps to be regarded as ſufficiently concluſive. When convulſions follow the injection of the ſolution, we can readily account for their doing ſo, independent of any action of the opium on the nerves of the heart. And when they do not, how are thoſe, who attribute theſe convulſions to what is termed ſympathy of the nerves, to account for their abſence, when the ſolution is injected into the heart, while the nerves of that organ, and thoſe of every other part of the ſyſtem, remain entire?

evacuated, it continued to contract with vigour. A little of the ſame ſolution uſed in the laſt experiment was then dropped into it.

No part of the ſolution, applied in this way, can be ſent through the arteries to the brain; but as all the nerves are left entire and uncompreſſed, if the convulſions which follow the injection of opium into the heart depend on any action of that drug on the nervous ſyſtem, they ought to be obſerved in this experiment.

On dropping the ſolution into the heart, it immediately ceaſed moving, but no convulſions ſupervened.

Leſt it ſhould be ſaid, that putting a ſtop to the circulation in the above experiments,

riments, prevented the nervous ſyſtem from undergoing the changes neceſſary for producing convulſions, the following was made.

The aorta in four frogs was ſecured by ligature, and the auricle wounded ſo as to permit the blood to eſcape; in other two, a ligature was thrown around all the veſſels attached to the heart; and this organ was removed. The ſcull of each was then perforated; and, after wounding the brain in the firſt four, a little of the weaker ſolution was dropped into it. In the other two, a few drops of a ſtronger ſolution were applied to the ſurface of the brain.

In all of them the muſcles of voluntary motion were ſeized with the moſt violent convulſions. They died, with preciſely the ſame ſymptoms which follow the injection of opium into the heart, when it paſses along the aorta.

On examining the ſtate of the muſcles after death, in the firſt four frogs, their irritability was found much impaired. I either did not examine the ſtate of the muſcles, after death, in the other two frogs, on which the experiment was made at a different time, or neglected to take notice of it in my notes.

The frogs uſed in this experiment were of different ſizes; two of the firſt four were full grown.

From theſe experiments, then, it appears, that opium, applied to the heart, is not capable of affecting any diſtant part, through the medium of the nervous ſyſtem.

Another perplexity, however, relating to the action of opium on the heart, ſtill remains to be unravelled.

Dr. Monro, it has been obſerved, found, that, by throwing a ſolution of opium into the cavity of the abdomen of a frog, the motion of the heart is almoſt immediately rendered leſs frequent; from which this author concluded, and certainly not without reaſon, that opium, applied to a diſtant part of the body, affects the motion of the heart through the medium of the nervous ſyſtem.

As this concluſion, however, contradicts the reſult of an experiment of Fontana's, above related, which was repeated much more frequently than Dr. Monro's, I ſuſpected that there had been ſome fallacy in the latter.

I therefore repeated Dr. Monro's experiment more than once, but found the reſult as he has ſtated it. The beating of the heart became leſs frequent, almoſt immediately on injecting the ſolution into the cavity of the abdomen.

It was ſtill plain, however, that both the concluſion which has been drawn from this experiment, and that which Fontana draws from his, could not be juſt, as they directly contradict each other.

There ſeemed little doubt of the juſtneſs of Fontana's concluſion. That of the other appeared more queſtionable. In the former,

mer, it is only maintained, that a certain effect is not produced by the opium, becauſe it is not obſerved to follow its exhibition; in the latter, it is not only maintained, that the opium produces a certain effect conſtantly obſerved to follow its exhibition, (an inference indeed as juſt as the other); but that it produces this effect in a particular way.

Theſe circumſtances led me to conſider, whether or not there is any other way, in which a ſolution of opium, injected into the cavity of the abdomen, can be ſuppoſed to influence the motion of the heart, beſides through the medium of the nervous ſyſtem, or that of the abſorbents.

A conjecture occurred to me, which is

confirmed by ſeveral of the following experiments, namely, that opium applied to the coats of the blood-veſsels, by deſtroying their muſcular power, (opium, it was found, deſtroys the power of action in all muſcles to which it is immediately applied), muſt affect the circulation in theſe veſsels; and conſequently, thrown into the cavity of the abdomen, influence the motion of the heart, by impeding, or entirely interrupting, that of the blood, in nearly one third of the whole animal; by which the ſupply to the heart is diminiſhed, and a greater than uſual obſtacle oppoſed to its perfect evacuation.

The firſt circumſtance, then, to be aſcertained, is, whether opium applied immediately, or nearly ſo, to the blood-veſſels of a living animal, impedes, or wholly interrupts, the circulation in theſe veſsels, independent of any general affection of the ſyſtem.

It is to be obſerved, that in the following experiment, the opium is not applied immediately to the coats of the blood-veſsels, but injected into a cavity, between which and theſe veſsels a denſe membrane of cellular ſubſtance is interpoſed. The ſkin of a frog, except in a few places, (chiefly the joints), does not adhere to the parts which lie beneath it.

Having adapted the web of a frog's foot to a microſcope, I injected eight or ten drops of a ſolution, (nearly as ſtrong as the ſtronger ſolution), under the ſkin of the leg.

In a few ſeconds the circulation became

came languid, and no motion could be perceived in ſome of the larger blood-veſſels. It gradually became more obſcure in the reſt, till, in the ſpace of about two or three minutes after the injection of the opium, it ceaſed altogether. Nor did this interruption of the circulation proceed from any general affection of the ſyſtem, ſince the motion of the blood ſtill continued in the other foot.

Leſt it might be ſuſpected that in applying the foot to the inſtrument, the veſſels were compreſſed, it is proper to obſerve, that the circulation in the foot after it was applied to the microſcope, continued as vigorous as natural, till the ſolution was injected. On another occaſion, indeed, I have obſerved, the circulation in the foot of a frog, applied

plied in the ſame way to the ſame microſcope, vigorous for ſeveral hours.

This experiment was made three times, in the ſame manner, and with the ſame reſult.

After determining that opium is capable of interrupting the circulation in the part to which it is immediately applied, independent of any general affection of the ſyſtem; all that is neceſſary in order to aſcertain whether it is in this way that it ſuddenly affects the motion of the heart, when thrown into the cavity of the abdomen, is to interrupt the circulation, and obſerve the effects of this drug applied in the ſame way, when it can only act on diſtant parts, through the medium of the nervous ſyſtem.

The functions of this ſyſtem, it has already been obſerved, are not impaired in the frog, for a conſiderable time after the circulation is interrupted *.

I ſlit the heart in ſix frogs, ſo as to permit the blood to eſcape freely; and in about a minute after, threw eight or ten drops

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* It may ſeem that I ſhould, in the firſt place, have ſhewn, that diminiſhing the quantity of blood, ſupplied to the heart, is capable of diminiſhing the frequency of its contractions. An experiment of this kind is perhaps unneceſſary, as the fact which it goes to prove is ſo generally admitted. But, that nothing may ſeem taken for granted, it will be found in the following experiment, that, after the ventricle of the heart was wounded, and thus a great part of the blood evacuated, the ſtruggles of the animal, which increaſed the flow of blood to the heart, never failed at the ſame time to increaſe the frequency of its contractions.

drops of the ſame ſolution, uſed in the laſt experiment, into the cavity of the abdomen, moving the tube, with which the injection was made, in various directions, that the ſolution might be applied as generally as poſſible. Little or none was returned.

In three of the frogs, the frequency of the heart's motion was the ſame after as before the injection of the ſolution; in the other three, it became leſs frequent about a minute after it.

There is room for conſiderable fallacy in this experiment. Cutting the heart may render its contractions more frequent than natural, and conſequently their frequency will diminiſh more rapidly than when the heart is left entire. Beſides, I always obſerved, that the ſtruggles of the animal, increaſing the ſupply of blood to the heart, increaſed the frequency of its contractions; and as this ſupply was always becoming leſs, their frequency, on this account alſo, would be conſtantly diminiſhing. It is extremely probable, that the diminiſhed frequency of the heart's motion, in three of the frogs, was not the effect of the opium, ſince it did not produce the ſame effect in the other three.

As it is poſſible, however, that ſome unperceived circumſtances might have counteracted the effects of the opium on the firſt three frogs, it was neceſſary to repeat the experiment in a more concluſive manner.

I obſerved, that although, on ſecuring the aorta by ligature, the heart is immediately diſtended with blood to a great degree, the frequency with which it beats after the operation, continues the ſame, or nearly ſo, for the ſpace of four or five minutes. It is increaſed when the animal ſtruggles; but there ſeemed no other circumſtance to influence the reſult of the laſt experiment, performed in this way; and it was eaſy to make allowance for this.

After ſecuring the aorta by ligature, therefore, in ſix frogs, and counting the beats of the heart, eight or ten, and in ſome fourteen or ſixteen, drops of the ſame ſolution uſed in the laſt experiment, were injected into the cavity of the abdomen, the tube being moved in various directions, as formerly. Little or none was returned.

When the animal ſtruggled, which moſt of them did the moment the injection was made, the frequency of the heart's motion was for a little increaſed. With this exception, it continued, in all of them, to beat with the ſame frequency after as before the injection of the ſolution, for the ſpace of four or five minutes; at the end of this time, it began to loſe ſeveral beats in the minute; but this was the conſequence of ſecuring the aorta, as I found by ſecuring this veſſel in other three frogs, without injecting any of the ſolution *.

The inference from theſe experiments is, that the diminiſhed frequency of the heart's motion, obſerved almoſt immediately on throwing a ſolution of opium into the cavity of the abdomen, does not proceed

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* The two latter experiments were made, becauſe, in Fontana's above alluded to, the opium was applied only to the ſtomach and inteſtines, while, in Dr. Monro's, it was thrown into the cavity of the abdomen, which might appear to ſome, perhaps, ſufficient to account for the difference of their reſults.

proceed from any action of the opium on this organ, through the medium of the nervous ſyſtem, but from its impeding, or entirely interrupting, the circulation, in nearly one third of the whole animal.

Opium immediately applied, even to the brain itſelf, although it excites violent and univerſal convulſions in the muſcles of voluntary motion, ſeems, from the following experiments, incapable of at all affecting the contractions of the heart.

I removed a piece of the cranium in two rabbits, about the ſize of a ſixpence, and as much of the dura and pia mater as I could, without injuring the brain. After replacing the teguments, and joining the lips of the wound by a ſuture, about a drachm and a half of a ſolution of opium in water was injected under the ſkin. This mode of applying the opium to the brain I found very convenient; it was ſuggeſted to me by a gentleman preſent when I made this experiment.

Soon after the injection of the opium, the animals were ſeized with violent convulſions. But the motion of the heart, which I examined from time to time, was not in the leaſt affected, except that it became more frequent when the muſcles of the limbs were alternately contracted and relaxed.

In the ſpace of ſome hours, the animals were reduced to a ſtate of great debility, the muſcles of voluntary motion being affected with a degree of paralyſis. But the motion of the heart ſtill continued ſtrong and regular.

I thought I felt a ſlight irregularity in its motion in one of theſe rabbits, about an hour before its death, near twenty-four hours after the ſolution of opium was injected. This I could not again perceive, although I frequently examined the motion of the heart afterwards.

On opening the thorax of this rabbit, a few ſeconds after its death, I found the heart contracting regularly. The contractions of the ventricles continued for near ten minutes, gradually becoming leſs vigorous. Thoſe of the auricles were ſeen for a much longer time.

This rabbit had been conſiderably debilitated the day before the experiment, by a quantity of opium thrown into its ſtomach.

The other was quite healthy, and had rather more of the ſolution applied to its brain. It died in nine hours.

The heart of this rabbit beat ſtrongly, and with perfect regularity, both during the ſpaſms, and ſubſequent paralyſis of the limbs. It was at laſt ſeized with uncommonly ſtrong convulſions, in which it almoſt inſtantly expired.

Immediately after its death, I applied my hand to the thorax, and felt the heart beating regularly for a few ſeconds. Its beats, when the hand was firſt applied, were little inferior in ſtrength to thoſe of the heart of a healthy rabbit. In the other, the motion of the heart could not be perceived, after death, from the outſide of the thorax.

It is a curious circumſtance, that at the time, the animals uſed in this experiment were thrown into convulſions by the ſlighteſt touch, their ſenſibility was ſo much impaired, that on running a knife through the foot of one of them, it ſhowed no ſigns of pain; only ſtarting convulſively, as it did when touched with the finger.

After removing a part of the cranium, and laying open the thorax, in ſeven frogs, a little of a ſolution of opium was applied to the brain, the muſcles of voluntary motion were ſoon ſeized with the moſt violent ſpaſms; but the motion of the heart continued perfectly natural, except when diſturbed by the convulſions of the trunk and limbs.

It has been obſerved, that, during the remiſſions of theſe convulſions, a very ſlight irritation is capable of renewing them. But on irritating the heart, even roughly, in this experiment, no irregular contractions could be excited in it.

Dr. Monro informed me, that he had, for ſome years paſt, performed the following experiment publicly in his Anatomical Theatre.

He injected a ſolution of opium in water, through a hole made in the cranium of a frog, in ſuch a manner that it paſſed along the ſpinal marrow, and part of it came out at a hole made in the lower end of the ſpine. By this mode of applying the opium, the animal was inſtantly killed.

An experiment, in which the nervous ſyſtem is ſo completely deranged by the action of opium, ſeemed well fitted for determining, whether this drug, applied to the brain and ſpinal marrow, is capable of directly influencing the motion of the heart. I therefore repeated the experiment in the following manner.

A hole was made in the cranium, and another in the lower end of the ſpine, in eight frogs; a ſtrong ſolution of opium, in water, was then injected through the hole made in the cranium, in ſuch a manner that it paſſed along the ſpinal marrow, and part of it came out by the hole in the ſpine.

Moſt of the frogs were deprived of ſenſe and motion as ſoon as the ſolution was injected; in two or three it was neceſſary to repeat the injection before the ſame effect was produced on them; and although they all appeared for ſome time quite dead, in the ſpace of two or three minutes moſt of them were ſeized with a trembling in the limbs, and ſome with ſtrong ſpaſms, which, during their intermiſſions, were not renewed by a ſlight irritation, as thoſe are which follow the application of opium to the brain only. I obſerved, however, that when they had not previouſly taken place, they were often excited by laying open the thorax. This was done in all the frogs uſed in this experiment; and in thoſe in whom it excited convulſions, or trembling, as well as in thoſe in which no motion whatever in the muſcles of the trunk or limbs took place, after the injection of the ſolution, the motion of the heart was found as vigorous as it is in healthy frogs *.

The ſolution uſed in this experiment muſt be ſufficiently ſtrong to deprive the animal of motion, at leaſt till the thorax is

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* A gentleman, who was preſent when I was making this experiment, having prepared a frog in the above manner, injected the cauſtic volatile alkali inſtead of the ſolution of opium. This alſo inſtantly deprived the animal of ſenſe and motion: he then laid open the thorax, and ſhewed me the heart uncommonly pale, and its motion conſiderably weaker than that of the heart in a healthy rabbit. I was inclined to attribute this affection of the heart, however, to the acrid vapour of the alkali, (in which the frog was immerſed, and which affected the eyes violently while we were examining the animal), being applied to this organ as ſoon as the thorax was laid open. I therefore laid open

is laid open; for I found in ſeveral other trials, that the uncommonly ſtrong ſpaſms induced on the limbs, when this is not the caſe, by rendering the circulation very irregular, and often, for ſome ſeconds, wholly interrupting it, greatly deranges the motion of the heart, by gorging it with blood; and ſeldom fails, more or leſs, to impair its vigour. So that, what at firſt ſight might ſeem a paradox, a ſmall quantity of opium, applied

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open the thorax of a healthy frog, and expoſed its heart to the ſame vapour, which immediately produced on it preciſely the ſame effects. We then repeated the above experiment in the following manner: Having injected the cauſtic volatile alkali as formerly, the animal was inſtantly deprived of ſenſe and motion. It was then carefully waſhed, that the vapour of the alkali, after the thorax was laid open, might not be applied to the heart, which was now found as vigorous as that of a healthy frog.

plied in this way, enfeebles the motion of the heart, while a larger quantity is incapable of at all affecting it.

The following manner of making this experiment is perhaps more concluſive: After making a hole in the cranium, and another in the lower part of the ſpine, the thorax was laid open, and the motion of the heart carefully obſerved in ſeven frogs; the ſolution was then injected as formerly, by which the animals were inſtantly deprived of voluntary motion, and appeared quite dead; but the motion of the heart was not in the leaſt affected; it continued with the ſame frequency and vigour, as before the injection of the ſolution.

All the frogs uſed in this experiment, ſome time after the injection of the ſolution,

lution, were ſeized with trembling, or convulſions, in the trunk and extremities.

I may obſerve, by the bye, that although irritating the brain mechanically, (like the application of opium to this organ), produces violent and univerſal convulſions in the muſcles of voluntary motion, both in frogs and rabbits; yet I have found, that in neither the one nor the other it affects the motion of the heart *. It would be digreſſing too far to conſider fully the inferences which theſe and many ſimilar obſervations ſeem to warrant.

It is ſufficient, in the mean time, to obſerve, that from the experiments which

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* Fontana makes the ſame obſervation reſpecting frogs.

which have been related, we arrive at this concluſion, that opium, applied to a diſtant part of the body, does not affect the motion of the heart, through the medium of the nervous ſyſtem; nor, on the other hand, does opium, applied to the heart, affect any other part of the body, through the ſame medium.

But the heart is not the only muſcle which opium, applied to a diſtant part, ſeems incapable of affecting, through the medium of the nervous ſyſtem.

Many conſiderations render it highly probable, that the ſame is true of all the muſcles of involuntary motion, without exception. That it is ſo of the muſcular coat of the alimentary canal, which, next to the heart, may be conſidered the chief of this claſs of muſcles, appears from the following experiment.

The abdomen in ſeveral healthy rabbits was laid open, and the periſtaltic motion of the inteſtines, which became very conſiderable a few ſeconds after they were expoſed to the air, carefully obſerved.

A large portion of the cranium was removed in another rabbit, and the brain cut acroſs its whole depth, in three directions. A ſmall part of it alſo, which, after the cuts were made, projected beyond the edges of the bone, was removed. A ſolution of opium in water was then injected into the brain, by means of a ſmall tube paſſed in various directions through its ſubſtance.

This was immediately followed by the

moſt violent and univerſal convulſions of the muſcles of voluntary motion, which, in the ſpace of a minute or two, became quite rigid, and as hard as a piece of board. The animal lay with its head drawn back, its limbs extended, in ſhort, affected with violent and complete tetanus.

In this ſituation, its abdomen was laid open, and the periſtaltic motion of the inteſtines found, in all reſpects, ſimilar to that obſerved in the other rabbits uſed in this experiment. I could not perceive that it was ſtronger or weaker, more or leſs irregular, in the one caſe than in the other.

On examining this rabbit, twenty-five minutes after the ſolution was injected into its brain, the muſcles of voluntary motion were found quite flaccid, and the animal dead. The motion of the inteſtines, however, was ſtill ſtrong in many parts of their tract, and continued ſo for thirty-ſix minutes longer, during which time I obſerved it. It was not again examined till forty-four minutes afterwards; the inteſtines were then cold and motionleſs.

In making this experiment, it is to be obſerved, that handling the inteſtines throws them into violent ſpaſms, whether opium be applied to the brain or not; and that thoſe parts which are moſt expoſed to the air loſe their motion ſooneſt: ſo that it is neceſſary to raiſe theſe, and examine the parts which lie beneath them, if we wiſh to aſcertain how long the periſtaltic motion continues.

This motion, I may obſerve, like that of the heart, is not in the leaſt affected by mechanically irritating the brain. In making this experiment, the animal muſt be well ſecured, otherwiſe the violent convulſions, induced on the muſcles of the limbs by toſſing the inteſtines, will increaſe the periſtaltic motion.

It has been ſhewn, that opium, applied to the external ſurface of the heart, very little, if at all, affects the muſcular power of this organ; applied, in conſiderable quantity, to its internal ſurface, it immediately deſtroys it. In like manner, applied to the external ſurface of the inteſtines, I could not be certain that it all diminiſhed the periſtaltic motion: on injecting it into their cavity, they almoſt inſtantly became paralytic *.

On comparing the experiments which have been related, particularly the firſt related, with thoſe in which opium thrown into the ſtomach and inteſtines, cavity of the abdomen, &c. is found to produce convulſions, it appeared probable, that in the latter caſes, as in the former, the convulſions do not proceed from any action of the opium on the nerves of the part to which we apply it, but from its being received into the ſanguiferous ſyſtem, and immediately applied to the brain.

And

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* From this effect of opium on the internal ſurface of the inteſtines, we are at no loſs to account for the coſtiveneſs which attends the uſe of this drug.

And this conjecture appeared the more probable, as the convulſions do not ſupervene for a conſiderable time after the exhibition of the opium, except when it is thrown into the ſanguiferous ſyſtem, or applied to the brain itſelf. In order to determine this point, and at the ſame time what effect opium produces, merely by its action on the nerves of the part to which it is applied, (if univerſal convulſions of the muſcles of voluntary motion be not this effect), I made the following experiments.

It has more than once been obſerved, that the nervous ſyſtem of the frog is capable of performing all its functions for a conſiderable time after the circulation is interrupted. A full-grown frog leaps about vigorouſly, for half an hour after the heart is cut out, by which not only the circulation is interrupted, but the greater part of the blood evacuated; And it generally continues to leap, when irritated, for more than twice that time.

All that was neceſſary, therefore, to determine the point in queſtion, was to cut out the heart, or otherwiſe interrupt the circulation, and then obſerve the effects of opium applied to the ſtomach and inteſtines, or injected into the cavity of the abdomen.

This experiment has been made, it was obſerved, by more than one author, and the reſult was general convulſions of the trunk and limbs.

As ſome unperceived circumſtance, however, might have influenced the reſult of theſe experiments, ſuch as, a ſmall quantity of the ſolution of opium having been accidentally applied to the ſkin, before the heart was removed, (ſee the 2d experiment with tobacco, at the end of this paper), as the experiments were made on but a ſmall number of frogs; and as thoſe who made them do not altogether agree concerning the part to which the ſolution muſt be applied, in order to induce convulſions, after the heart is removed, I thought it worth while to repeat the experiment on a larger ſcale.

After cutting out the hearts of 24 frogs, a ſolution of opium in water was injected into the ſtomach and inteſtines of ſome of them, and into the cavity of the abdomen of others. The following are the particulars relating to each. The ſtrong ſolution was uſed, except when the contrary is mentioned.

Into the 1ſt, not full grown, 30 drops were injected; it died in half an hour: Into the 2d, not full grown, the ſame quantity; it died in 35 minutes: Into the 3d, the ſame quantity; it died in 51 minutes: Into the 4th, very young, 10 drops; it died in 25 minutes: Into the 5th, almoſt full grown, 30 drops; it died in an hour: Into the 6th, full grown, 30 drops; it died in 55 minutes: Into the 7th, full grown, 60 drops; it died in an hour and two minutes: Into the 8th, full grown, 60 drops alſo; 8 or 10 were returned; it died in 58 minutes: Into the 9th, not quite full grown, 30 drops of the weaker ſolution; the time of its death was not obſerved: Into the 10th, very young, 10 drops of the weaker er ſolution; it died in 54 minutes: Into the 11th, not full grown, 50 drops of the ſame ſolution; part was returned; the time of this frog's death was not obſerved: Into the 12th, very young, 10 drops of the ſame ſolution; part was returned; the time of its death was not obſerved: Into the 13th, not full grown, 26 drops of the ſame ſolution; it died in 59 minutes: Into the 14th, nearly full grown, 63 drops of the ſame ſolution; part was returned; it died in 52 minutes: Into the 15th, 20 drops of a ſolution nearly as ſtrong as the ſtrong ſolution: Into the 16th, 15 drops of the ſame ſolution; about 3 were returned; the time of the death of neither of the two laſt frogs was obſerved.

Solutions of various ſtrengths were injected into the eight remaining frogs; into ſome a weaker, into others a ſtronger ſolution, than that employed in any of the above caſes.

Thoſe which were of the ſame ſize, generally died the ſooner, the greater the quantity of opium which had been injected. Young frogs die much more readily from injuries of this kind, than thoſe which are full grown, as may be ſeen from ſeveral parts of this experiment.

The manner in which all theſe frogs died was preciſely the ſame: Soon after the injection of the opium, they were ſeized with a degree of langour, generally proportioned to the quantity injected. This, in moſt of them, went off to a greater or leſs degree, in the ſpace of ſome minutes. They again, more gradually,

dually, became languid, and growing more and more ſo, imperceptibly died, without the ſlighteſt convulſion in any part of the body. I neglected to examine the ſtate of the muſcles, after death, in the fourth frog uſed in this experiment; in all the others, they were found to contract readily, on wounding the nerves which terminate in them.

Fifty drops of a very ſtrong ſolution of opium in water, conſiderably ſtronger than the ſtrong ſolution, was injected into the cavity of the abdomen, of one of the laſt eight frogs, full grown, the heart, as in the other caſes, having been previouſly cut out. Part of the ſolution was returned when the animal moved.

For a few ſeconds after the injection of the ſolution, it leaped about with vigour;

gour; in a ſhort time, however, it ſeemed incapable of leaping; and in the ſpace of two minutes, was almoſt quite deprived of motion. It ſoon began to move again, and in eight minutes could leap about. Fifty-one minutes after the injection of the ſolution, it leaped on being much irritated. Twenty-eight minutes after this, it turned itſelf when laid on its back. It died in about an hour and twenty-eight minutes after the injection of the ſolution.

I have related this inſtance particularly, as it is remarkable for the great degree of langour which followed the injection of the opium, and for the length of time which the animal, notwithſtanding this, ſurvived the application of that drug.

The foregoing experiment was repeated in the following manner. The thorax was laid open in eight frogs, and a ligature thrown around all the veſſels attached to the heart: This organ was then removed, with the loſs of no more blood than it happened to contain at the time the ligature was thrown around the veſſels. A ſolution of opium was then injected into the cavity of the abdomen in all of them, through a hole made in the muſcles.

The ſolution injected into the firſt 6, was not quite ſo ſtrong as the ſtrong ſolution; that injected into the 7th and 8th, was ſtronger. All the frogs uſed in this experiment, except the 6th, were full grown. Into the 1ſt, 16 drops were injected: Into the 2d, 20 drops; about 2 or 3 of which were returned: Into the

3d, 16 drops; about 3 were returned: Into the 4th, 25 drops; about half was returned: Into the 5th, 8 drops: Into the 6th, 30 drops; part of which was returned: Into the 7th, 12 drops; part was returned: Into the 8th, 14 drops.

The frogs uſed in this experiment died in preciſely the ſame manner as thoſe uſed in the laſt. The muſcles of their limbs contracted readily after death, when the nerves terminating in them were irritated.

It appears from theſe experiments, that the effect of opium, when it acts on the nerves of the part to which it is applied, is merely that of inducing a general languour, which, if the quantity applied be conſiderable, terminates in death. This effect of opium does not eſſentially differ from that of any other topical irritation *.

From all that has been ſaid, it appears, that the various effects of opium on the living animal body may be divided into three claſſes. The firſt, comprehending its action on the nerves of the part to which it is applied, not differing eſſen-

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* In man it has been ſhewn, that a large doſe of opium produces ſleep, merely by its action on the nerves of the part to which it is applied ; ſo do other topical irritations (mechanical injury not excepted), though more ſlowly. If it be this effect of opium which Dr. Whytt alludes to, when he ſays, that opium deſtroys the power of motion in every part of a frog, as ſpeedily after as before the exciſion of the heart, the obſervation is certainly juſt. From the nature of the experiments from which he draws the concluſion, however, he does not ſeem to allude to this effect of it.

tially from that of any other topical irritation. It is doubtful whether the ſhock given to the ſyſtem, merely by the action of opium on the nerves of the part to which it is applied, has ever been ſufficient to kill. I have never ſeen it produce ſo remarkable an effect in any other caſe as in one above related.

A large quantity ſuddenly applied to a very extenſive ſurface, may be capable, perhaps, of inſtantly killing animals leſs tenacious of life than frogs are. A variety of ſtrong impreſſions, that produced by receiving a large quantity of ſpirit of wine into the ſtomach, of very cold water when the body is overheated, &c. are well known to have occaſioned ſudden death. It ſeems to be a general law of the animal œconomy, that the firſt effects of a ſtrong irritation are very violent; but if theſe be withſtood, it is afterwards borne with leſs inconvenience. It has juſt been ſhewn, how ſtrikingly true this is of the effects of opium, when it acts only on the nerves of the part to which it is applied.

The ſecond claſs into which the effects of opium may be divided are, its effects on the heart and blood-veſſels; that of increaſing their action, when applied in ſmall quantity *; and that of impairing

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* It has been obſerved, that a ſhort time after we take a moderate doſe of opium, the pulſe becomes quicker and fuller; an effect, which, from the experiments that have been related, can only proceed from the opium being abſorbed and immediately applied to the heart; ſince it has been proved, that opium cannot affect the motion of this organ through the medium of the nervous ſyſtem.

or altogether deſtroying their power of action, when applied to them more freely [*]. In neither of theſe effects, however, does the action of opium differ eſſentially from that of many other ſubſtances. Are not moſt acrid ſubſtances, in ſmall quantity, capable of exciting ſtrong contractions in the muſcular fibre, and of deſtroying its power of action, when applied more freely [†]? Even mechanical irritation, applied in different degrees, produces the ſame effects.

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[*] It does not appear, that, by the largeſt doſe, we can ſo increaſe the quantity of opium abſorbed, that it is ſufficient to deſtroy the muſcular power of the heart, merely by its action on that organ. It may be ſafely aſſerted, perhaps, that opium never kills by deſtroying the muſcular power of the heart, except when injected into it, or into the blood-veſſels.

[†] But the tendency of different ſubſtances to increaſe or deſtroy the action of the muſcular fibre is different

The third claſs, into which the effects of opium may be divided, comprehends thoſe it produces when immediately applied to the brain. When the doſe is moderate, impaired ſenſibility, langour, ſleep: Effects obſerved in a greater or leſs degree, from other gentle irritations applied to this organ, and which we do not perceive from a moderate doſe of opium, till we know from the ſymptoms it produces, compared with the foregoing experiments, that it has been conveyed to the heart; from which, in the courſe of circulation, it is ſent to the brain, as

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different. Tobacco, for inſtance, is more apt to deſtroy, and leſs apt to increaſe, its action, than opium.

well as to the other parts of the body. What ſhare its action on the latter parts has in producing theſe effects, it is impoſſible to ſay. We have reaſon to believe it but trifling. It appears from the experiments juſt related, that no part of them is to be aſcribed to its action on the heart itſelf*.

Opium, applied more freely to the brain, produces the ſame effects which moſt violent irritations, immediately applied to this organ do, convulſions and death *. But the convulſions produced by opium, it has been ſhewn, are of a peculiar kind. In each of its effects on the living animal, we ſtill find that opium has much in common with other ſubſtances, but, at the ſame time, ſome thing peculiar to itſelf.

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* The increaſed determination of blood to the head indeed, in conſequence of the ſtronger action of the heart, is found to diſpoſe to ſleep; but this, in the preſent caſe, may be overlooked, as the effects of the opium applied to the brain are ſo much more conſiderable.

It may appear an omiſſion, not ranking among the effects of opium received into the ſyſtem, thoſe it ſeems to produce on the muſcles of voluntary motion. In ſome of the foregoing experiments, the irritability of theſe muſcles was found much impaired after death; although the opium was not applied di-

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* Opium does not always prove fatal, when it produces convulſions. I have ſeen a rabbit recover after violent convulſions induced by a large doſe of this drug.

rectly to the muſcles themſelves. The reaſon of this ſeeming omiſſion will appear from the following obſervations.

Comparing Fontana's experiment (in which he found the irritability of the muſcles as little impaired by the action of opium applied to the ſtomach and inteſtines of the entire animal, as to thoſe of one with the heart cut out), with others which have been related, we ſhould infer, that the preſence of opium in the ſyſtem ſcarcely, if at all, affects the irritability of the muſcles of voluntary motion. From Dr. Alexander's experiments, on the other hand, we muſt conclude, that they are wholly deprived of their irritability by that drug, whether it be received into the ſyſtem by means of the abſorbents, or act merely on the nerves of the part to which it is directly applied.

Were I to truſt to the accuracy of my own obſervations, I ſhould diſſent from both opinions. I have never found the irritability of theſe muſcles wholly exhauſted by opium, applied in any manner, except to the muſcles themſelves. Nor have I found their irritability as little affected by the application of opium to the ſtomach and inteſtines of the entire animal, as to thoſe of one with the heart cut out.

Upon the whole, the reſult of my experiments on this part of the ſubject has been, that if opium occaſions convulſions, it impairs the irritability of the muſcles of voluntary motion; if it does not, their irritability is not in the leaſt affected by it.

From which it appears probable, that the impaired irritability of theſe muſcles, obſerved in the former caſe, is the conſequence of the violent contractions excited in them by the irritation applied to the brain, and not of any action of the opium on the muſcles themſelves. In order to determine the truth or fallacy of this opinion, I made the following experiment.

After injecting either into the ſtomach and inteſtimes, or into the cavity of the abdomen, I forget which, (for I have loſt the notes of this experiment), of two frogs, equal in ſize and vigour, the ſame quantity of opium; the one was kept free of every thing which, during the remiſſion of the convulſions, might tend to renew them; ſo that they were rendered as moderate, and the remiſſions as long, as poſſible; in the other, as ſoon as a remiſſion took place, the convulſions were renewed by ſlightly touching it; ſo that, although both frogs had taken the ſame quantity of opium, yet the one was affected with more violent and permanent convulſions than the other.

If, then, the impaired irritability of the muſcles of voluntary motion, obſerved after death, when an animal is killed by opium, depends on the preſence of this drug in the ſyſtem, the ſtate of theſe muſcles in both the frogs uſed in this experiment ſhould be found the ſame. If it be the conſequence of the contractions excited in the muſcles, it ſhould be more obſervable in the one frog than in the other.

The latter was found to be the caſe, in a very remarkable degree. I do not exactly remember how often this experiment was repeated; but recollect that it was not made above two or three times; ſo that its reſult can ſcarcely be regarded as certain. Some other experiments have been related, however, which tend to prove the ſame thing.

It was obſerved, that both Dr. Alexander and Dr. Fowler have ſhewn, that if the nerves going to any limb be divided before the ſolution of opium is exhibited, the muſcles of this limb are neither affected with convulſions previous to death, nor is their irritability found impaired after it. Yet the opium is conveyed to them, in the courſe of circulation, as well as to thoſe of any other part of the body.

The teſt of the degree of irritability remaining in the muſcles after death, which was uſed in the foregoing experiments, is doubtleſs a very groſs one. A nice teſt in theſe experiments would have been of little conſequence, however; ſince the irritability ſeems affected by circumſtances ſo various, that, without an infinite number of experiments, we could not aſcertain to what the ſmall differences, detected by ſuch a teſt, are owing.

The influence, diſcovered by Galvani, appears at firſt ſight an excellent teſt of the degree of irritability remaining in muſcles, and has been uſed as ſuch; but its laws ſeem at preſent too little known to permit us to employ it with much confidence in phyſiological inquiries.

I am inclined to believe, that a certain ſtate of the nerves may prevent this influence producing contractions in muſcles, even while their irritability remains; at leaſt I found, that although mechanical irritation excited ſlight contractions in the muſcles of a limb, whoſe nerves had been divided about a week before the death of the animal *; yet none could be produced in them, by the influence diſcovered by Galvani. Inſtances might be adduced, in which the employment of this influence in phyſiological

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* It is found, that the ſtructure of a nerve is altered, even to the naked eye, when it has been divided for ſome time before the death of the animal.

ſiological inquiries has already led to erroneous inferences, from our not being ſufficiently acquainted with its laws.

The circumſtances which ſeem chiefly to influence experiments, made on the irritability of frogs with the groſs teſt I employed, are, *1ſt*, Their age, the irritability of young frogs being much more readily exhauſted than that of ſuch as are full grown. *2dly*, Their death being ſudden or lingering, the latter leaving the irritability more impaired than the former. *3dly*, The time which the frogs are kept after being brought from the fields. The more vigorous frogs are, the more irritability their muſcles poſſeſs. *4thly*, Throwing ligatures around the limbs. If a tight ligature be thrown around a limb, and kept applied for twenty minutes, or half an hour, immediately before the death of the animal, all the muſcles beyond the ligature are found, after its death, quite void of irritability.

This cannot be attributed to the ligature preſſing on the nerves of the limb, and cutting off its free communication with the brain, ſince dividing the nerves does not produce the ſame effect. It ſeems to depend on an accumulation of blood taking place in the muſcles, (which are always found very red), owing to its return by the veins being prevented.

This fact ſuggeſts an experiment, by which it may be determined, perhaps, whether or not the irritability of the muſcles be derived from the nervous ſyſtem. For if it be found, that, when the muſcles of a limb are thus deprived of their irritability, (which they may readily be during the life of the animal), it can be reſtored, after all the nerves going to the limb are divided, there will then be little doubt of its being derived from ſome other ſource. I have made this experiment, but not in ſo ſatisfactory a manner, that any certain concluſion can be drawn from it.

THE doctrine of the ſympathy of nerves has been ſo much employed in accounting for the effects of opium, that a few obſervations upon it here may not be improper. Although there is ſcarcely any doctrine in medicine at preſent more implicitly received, it ſeems far from being fully eſtabliſhed *.

The phenomena which have been referred

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* The following opinions concerning this doctrine were laid before the Royal Medical Society of Edinburgh, and ordered to be inſerted in their books, on the 1ſt of February 1794. I mention this circumſtance, becauſe a work has appeared ſince the above date, in which, although the author maintains very different opinions on this head, there are one or two hints thrown out, to which, it might be thought, I ſhould own ſome obligation.

ferred to the ſympathy of nerves, are thoſe in which an involuntary motion, or a ſenſation, is produced in any part of the body by an irritation applied to the extremities * of the nerves, not of that part, but of ſome other; ſuch as the motion of the diaphragm in ſneezing, pro-

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* A ſenſation produced in any part, by ſtretching or compreſſing the trunk of the nerve which terminates in it, is no inſtance of the ſympathy of nerves. If a nerve going to any part be compreſſed, the feeling of that part muſt be impaired. If a nerve be ſtretched, there muſt be a pain referred to its extremities, for the ſame reaſon that, were we to pull a muſcle, we ſhould excite a pain at its inſertions. Is it a juſt inference from theſe facts, that an injury applied to the nerves of a ſtump will excite a pain referred to the extremity of the member that is loſt? Has not confounding theſe facts with others referred to the ſympathy of nerves, to which they bear no analogy, tended to perplex this ſubject?

duced by an irritation of the nares, a pain felt in the glans penis from an affection of the bladder *," &c.

Theſe phenomena, then, may be divided into two claſſes; thoſe in which *ſenſation*, and thoſe in which *motion*, is the reſult. I ſhall, in the firſt place, conſider the former, becauſe under it the more numerous ſet of facts are included; and becauſe, what I ſhall ſay of this claſs will be found uſeful in ſpeaking of the other.

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* With regard to thoſe caſes of ſympathy in which the muſcles of involuntary motion only are concerned, they do not fall to be conſidered here; ſince, in the preſent ſtate of our knowledge, there is not a ſhadow of reaſon for attributing them to any connection of nerves.

The following queſtion is the firſt that preſents itſelf, concerning which there can ſcarcely be two opinions. In what part of the ſyſtem does that change take place, which is the immediate cauſe of ſenſation?

The immediate cauſe of ſenſations, either exiſts in the various parts to which they are referred, demonſtrating that the ſenſorium commune pervades the whole ſyſtem; or it does not, demonſtrating that the cenſorium commune is confined to a particular part of the ſyſtem, to which every impreſſion cauſing ſenſation is conveyed. Since one of theſe poſitions muſt be juſt, in order to eſtabliſh either, it is ſufficient to ſhow, that the other is not. The queſtion, then, reſolves itſelf into this, Does the immediate cauſe of ſenſations exiſt in the parts to which they are referred ?

When a man complains of a pain in the toes, after the limb has been amputated, is the immediate cauſe of the ſenſation in the part to which it is referred, or elſewhere ? No body can heſitate in anſwering this queſtion. We have, therefore, an unequivocal inſtance, in which the immediate cauſe of ſenſation does not exiſt in the part to which it is referred.

But this is not a ſolitary fact, it is a general law of the animal œconomy, that we continue to refer various ſenſations to any part of the body, which is ſuddenly loſt for ſome time after it is ſo. The fact is as evident in the loſs of a finger, or in that of a tooth, as in the loſs of a limb. Nor can it be ſhewn, why the immediate cauſe of ſenſation ſhould ſo exiſt in theſe caſes, and not in all.

From direct experiment, then, the concluſion is unavoidable, that the immediate cauſe of ſenſations does not exiſt in the parts to which they are referred, but in ſome other; that is, the ſenſorium does not pervade the whole ſyſtem, but is confined to a particular part of it; and having advanced thus far, we know, from numberleſs obſervations, that this part is lodged ſomewhere within the cranium in man, and, by analogy, in the animals that reſemble man. In ſome animals it ſeems partly lodged in the ſpine. It is this part, then, which is meant by the term ſenſorium commune, wherever it occurs in the preſent paper.

The next queſtion which preſents itſelf is, If the immediate cauſe of ſenſation exiſts in the ſenſorium commune, why do we very conſtantly refer the ſenſation to the part of the body on which the impreſſion, cauſing it, is made *.

When we look at the various objects that ſurround us, why do we refer one to the diſtance of two feet, another to that of three, and ſo on ? For no other reaſon,

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* The mode of reaſoning employed in conſidering this queſtion, though different, is ſimilar to, and was ſuggeſted by, what Hartley ſays of the manner in which we refer ſenſations to particular parts of the body. See his Theory of the Human Mind.

reaſon, but that experience has taught us to connect certain ſenſations with certain diſtances. When we ſee two objects which we know to be nearly of the ſame tangible extenſion, for inſtance, two men, and yet obſerve, that the one occupies but the fourth of that part of the viſible plain which is occupied by the other, we judge the former to be at twice the diſtance of the latter; if the former occupy but the ninth part of that ſpace occupied by the other, we judge him to be at three times the diſtance; and ſo on. The degree of faintneſs, the number of intervening objects, and a few other circumſtances, occaſionally aſſiſt us when we judge of the diſtance of objects by the eye. But none of theſe circumſtances are eſſentially connected with diſtance; it is only experience which has taught us to connect them in our minds.

Preciſely the ſame thing takes place in the other caſe; there is no particular ſenſation eſſentially connected with any particular part of the body; but experience has taught us to connect certain ſenſations with certain parts *: ſo that to the ſenſation ariſing from every impreſſion, there is ſomething as it were ſuperadded, which we have conſtantly obſerved attend all impreſſions made on the ſame part; and it is this which teaches us to refer the ſenſation to that part; in the ſame manner as there is ſomething, for inſtance,

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* For the manner in which we at firſt diſcover the ſeat of impreſſions, ſee Hartley on the Human Mind, aud others.

inſtance, the degree of faintneſs, ſuperadded to the appearance of all bodies at the ſame diſtance, which teaches us that they are at that diſtance.

And as, in the latter caſe, according to a well-known law of the animal œconomy, we attend to the diſtance of an object, overlooking the means by which we acquire a knowledge of its diſtance; ſo, in the former caſe, we attend to the injured part, overlooking the means by which we determine its poſition with reſpect to other parts of the body.

Is it ſaid, that we have a power of referring ſenſations to particular parts of the body, independent of experience? The following ſimple experiment is ſufficient to convince us that we have not. I have frequently made the experiment, ſince I firſt heard of it from a gentleman of my acquaintance.

We refer ſenſations with little accuracy to parts of the body which we are not much accuſtomed to ſee, or otherwiſe diſtinguiſh from each other. If a perſon blind his eyes, and deſire another to touch one of his ſmall toes, he will find it quite impoſſible to tell which of them the perſon touches, and will not gueſs right much oftener than he would do, were the other touching one of four things quite unconnected with his body.

We arrive, then, at this concluſion, that the immediate cauſe of ſenſations exiſts in the ſenſorium commune; and that they are referred to the parts, on which the impreſſions cauſing them are made, by experience alone.

We have all perceived, that the ſenſation ariſing from a pretty ſtrong impreſſion is not confined to the very ſpot to which the injury is applied, but is felt, at the ſame time, in ſurrounding parts.

It is alſo a fact, that the more ſenſible any of the ſurrounding parts is; the more, in general, it partakes of the ſenſation. Thus, in a perſon labouring under the ſtone in the bladder, the whole hypogaſtric region is pained. But the end of the urethra, glans penis, and teſticle, parts endowed with very keen feeling, partake more of the ſenſation than any other.

By how many injuries applied to diſtant parts, is the ſtomach affected, which is perhaps the moſt ſenſible part of the ſyſtem ?

Inflamed ſores, where there is a morbid degree of ſenſibility, are excellent examples of the ſame thing. If any part near ſuch a ſore be injured, the pain is felt more acutely in the ſore than in the other neighbouring parts *.

But it is likewiſe a fact, that when any of the parts in the neighbourhood of that

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* The pain in affections of the liver being referred to the ſhoulder, and not to the ſtomach, the more ſenſible neighbouring part, ſeems an exception to the general rule. But it appears from many inſtances, that thoſe parts are moſt apt to ſympathiſe, which lie nearly in the ſame line from the brain. This, it is more than probable, is owing to ſuch parts being ſupplied with nerves from neighbouring parts of this organ. We meet with idioſyncraſy in this as in other functions of the ſyſtem. I ſhall preſently have occaſion to mention an inſtance of this kind; many others might be adduced.

on which the impreſſion is made, is a part of very acute feeling, while the injured part itſelf is one of comparatively dull feeling, the ſenſation excited in the former is often more intenſe than that excited in the latter.

We have inſtances of this in both the caſes juſt ſtated: the pain excited in the ſore is often more acute than that excited in the injured part, in its neighbourhood; and that excited in the urethra, glans penis, and teſticle, than the pain felt in the region of the bladder. When this takes place, as we attend to the ſtronger impreſſion, and neglect the weaker, the former only is felt.

In all ſuch caſes, we refer the ſenſation from a leſs to a more ſenſible part; yet it is not at all times wholly confined to the latter; for when we attend particularly to the ſeat of the impreſſion, we generally feel a ſenſation there, as well as in the more ſenſible diſtant part; but one ſo faint, that it is overlooked while the ſtronger ſenſation is preſent, except we endeavour to perceive it.

All that is here ſaid is well illuſtrated by the following experiment, which I accidentally hit upon ſome years ago. I found, that by roughly irritating the umbilicus, a part endowed with very dull ſenſation, I could excite a pain at the end of the urethra *. As the irritation

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* I mentioned this circumſtance to a gentleman of my acquaintance, who, on pinching the umbilicus, felt a pain along a great part of the urethra. I have mentioned it to others, who experienced no ſuch effect from irritating this part.

was increaſed, this pain gradually became very acute. There was alſo a dull ſenſation of general pain in the lower belly, ſimilar to that produced when the teſticle is ſlightly injured, which remained for ſome time after the irritation was withdrawn. Having made the experiment frequently in the ſpace of ten or twelve minutes, I may obſerve by the bye, a conſiderable degree of ſickneſs at ſtomach was produced, and a ſenſation I cannot well deſcribe; which was ſo diſagreeable, that I have not ſince prevailed on myſelf to repeat this experiment.

I conſtantly obſerved, in making it, that when the pain at the end of the urethra was conſiderable, the irritation was not felt at the umbilicus, although I could always perceive it, by bending my attention to this part.

Upon the whole, then, we find, that the ſenſation is not always confined to the part on which the impreſſion is made; that it is felt in ſurrounding parts, with various degrees of intenſity, generally proportioned to their degrees of ſenſibility; and that it is ſometimes more acute in the more ſenſible neighbouring parts, than in that to which the injury is applied.

But it has been ſhewn, that the immediate cauſe of every ſenſation exiſts, not in the part to which it is referred, but in the ſenſorium commune; and that the ſenſation is referred to the former, by experience alone.

Comparing theſe facts, the concluſion is unavoidable, that the phenomena, which are ſaid to depend on the ſympathy of nerves, as far as relates to thoſe inſtances in which ſenſation only is concerned, proceed from certain changes induced on the ſenſorium commune, and depending on the two following circumſtances; namely, different parts of the ſenſorium being endowed with different degrees of ſenſibility, and a change occaſioned in one part being capable of inducing a ſimilar change in ſome other; the ſenſations cauſed by ſuch changes, being each referred to its correſponding part of the body, in the manner above explained.

The application of the principles juſt laid down, to explain particular caſes, in which the phenomena in queſtion take place, is in general ſo evident, that it requires no illuſtration. I ſhall conſider the only inſtance in which it is not ſo. One I have already had occaſion to mention, in which we refer the ſenſation to a part that is ſeparated from the body; and I ſhall take as an example of this, a perſon complaining of a pain in the toes, after the leg has been amputated.

Provided certain cauſes, capable of giving us a ſenſation, which we have been accuſtomed to refer to a certain part of the body, ſtill continue to act, the ſenſation will be referred thither, whether the part itſelf exiſts or not, till a new experience overcome the former, and teach us not to refer any ſenſation to a part that is now loſt.

It is evident from what has been ſaid,

that after the amputation of a limb, there ſtill may exiſt in the body, cauſes capable of giving us ſenſations which we have been accuſtomed to refer to this limb; for we have been accuſtomed to refer to it, not only ſenſations from impreſſions made on the limb itſelf, but thoſe from impreſſions made on parts in its neighbourhood. The pain excited by the irritation at the end of the ſtump, therefore, is referred to that part of the limb we have loſt, as well as to the part which remains.

But it has been ſhewn, that of the parts in the neighbourhood of that on which the impreſſion is made, thoſe partake moſt of the ſenſation which are endowed with the keeneſt feeling. Of all the parts of the inferior extremities, the toes are the moſt ſenſible: on this account the injury done to the limb is felt more ſeverely in them than in any other part of it.

None of us would be ſurpriſed to find a perſon complaining of a pain in the toes, from a wound in any part of the leg, while it ſtill remains attached to the body; yet, if the facts which have been ſtated be juſt, (and that they are ſo cannot, I believe, be queſtioned), the pain, in both caſes, is referred to the toes, for preciſely the ſame reaſon *.

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* Speaking of a certain hypotheſis, Dr. Darwin obſerves, in the 3d ſection of his Zoonomia, "There "is another objection, that at firſt view would ſeem "leſs eaſy to ſurmount. After the amputation of a "foot or a finger, it has frequently happened, that an "injury being offered to the ſtump of the amputated limb

With regard to the caſes referred to ſympathy of nerves, in which motion is the reſult, it may be obſerved, we every hour ſee the ſenſorium affected by impreſſions made on the nerves; and the conſequence motion in various parts of

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"limb, whether from cold, too great preſſure, or "other accidents, the patient has complained of a "ſenſation of pain in the foot or finger that was cut "off. Does not this evince that all our ideas are excited in the brain, and not in the organs of ſenſe? "This objection is anſwered by obſerving, that our "ideas of the ſhape, place, and ſolidity of our limbs, "are acquired by our organs of touch and ſight, "which are ſituated in our fingers and eyes, and "not by any ſenſations in the limb itſelf."

But how are ſenſations from impreſſions made on the ſtump aſſociated with any idea of the fingers or toes? Such ſenſations have been aſſociated with the idea of the body, univerſally aſcribed to the change produced in this part of the ſyſtem. But why do we ſelect certain motions, ſneezing, vomiting, &c. excited by ſimilar impreſſions, and alledge that they depend on other laws? Becauſe the

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idea of that part at which the limb was amputated. Dr. Darwin obſerves, indeed, in the next paragraph, "In this caſe the pain or ſenſation, which formerly "has ariſen in the foot or toes, and been propagated along the nerves to the central part of the "ſenſorium, was at the ſame time accompanied with "a viſible idea of the ſhape and place, and with "a tangible idea of the ſolidity of the affected limb: "now, when theſe nerves are afterwards affected by "any injury done to the remaining ſtump with a ſimilar degree or kind of pain, the ideas of the ſhape, "place, or ſolidity of the loſt limb, return by aſſociation; as theſe ideas belong to the organs of

ſight

latter motions are involuntary. They are not wholly ſo, however; both vomiting and ſneezing can often for a certain time be interrupted by the will. Beſides, they are frequently interrupted, and

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" ſight and touch on which they were firſt exci-" ted."

No farther ſuppoſition would ſeem requiſite, were it aſcertained, that after a leg is cut off, the irritation at the end of the ſtump is applied to the trunks of thoſe nerves only that terminated in the part of which the patient complains, chiefly the toes. But we know that the irritation is applied to the cut ends of all the nerves which went to any part of the amputated limb; ſo that, were Dr. Darwin's explanation juſt, not the idea of the toes only, but that equally of every part of the limb, ſhould be aſſociated with the pain at the end of the ſtump.

and vomiting even produced, by a ſtrong affection of the mind. And are there not other motions generally admitted to depend on an affection of the ſenſorium commune, which have the ſame right to be referred to the ſympathy of nerves? Tickling the ſides, or ſoles of the feet, excites violent and completely involuntary motions. Yawning too, and many other ſimilar motions, might be adduced as inſtances of the ſame kind.

But laying this mode of reaſoning aſide, if it be granted, that the motions which have been referred to ſympathy of nerves are not independent of the ſenſations which precede them, (and no body, I believe, will aſſert that they are), it is a corollary from what was ſaid of the caſes of ſympathy, in which ſenſation is the reſult, that theſe motions proceed from affections of the ſenſorium commune.

Dr. Monro, who has paid more attention to this ſubject than moſt other authors, was led, by many obſervations, to this concluſion, " That, in general, the nerves of the body ſympathiſe, not from their connection in their progreſs, but from their connection at their origin." I would only go a ſtep farther, and ſay, that the nerves always ſympathiſe from their connection at their origin; which is the ſame as ſaying, that no ſuch thing as the ſympathy of nerves exiſts, and that all the phenomena, which have been referred to this ſuppoſed law, depend on affections of the ſenſorium commune.

But granting (it may be ſaid) that the immediate cauſe of all theſe phenomena exiſts in the ſenſorium commune, if it be found that thoſe parts are moſt apt to ſympathiſe, between which there is the moſt evident connection of nerves, the connection of nerves muſt be regarded as a mediate cauſe of the phenomena in queſtion. But how ſlight, in many inſtances, is this connection between parts which ſympathiſe moſt? And where do we find it ſo evident as between parts which very rarely ſympathiſe? What part, then, do the nerves act in the production of theſe phenomena? No other than they act in the production of all phenomena in which they are concerned, that of conveying impreſſions to the ſenſorium, or of conveying a ſomewhat (to uſe Dr.

Monro's expreſſion, in the preſent ſtate of our knowledge the beſt perhaps, we can uſe) from the ſenſorium to the muſcles of voluntary motion.

APPENDIX.

EXPERIMENTS, made with a view to determine the manner in which Tobacco acts on the Living Animal Body.

THE following Experiments may be deemed an uſeful addition to this Paper, becauſe they both tend to confirm the reſults of thoſe which have been related, and to eſtabliſh ſome points concerning the action of tobacco on the living animal body.

The ſolution which was uſed in theſe experiments was prepared by expoſing two ounces of tobacco with ſix ounces of water, in a phial carefully corked, to a temperature of 90°. for twenty-four hours *. It was then filtered, and near ſix ounces of a ſtrong ſolution obtained, which appeared black in a common two-ounce phial.

A few drops of this ſolution were injected

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* This mixture was expoſed to the temperature mentioned for twenty-four hours only, as the active parts of tobacco are readily extracted by water, and I had found, from a former trial, that it is very apt to become putrid at ſo high a temperature.

jected into the heart in four frogs, through a hole made in the auricle. The heart inſtantly became paralytic, and the animals were ſeized with the moſt violent trembling, and a complete loſs of ſenſe and motion in the eyes and fore-limbs: in ſome, the head was drawn back; and in all, every joint of the hinder-limbs was convulſively bent to the utmoſt; juſt the contrary of what happens in the extremities, when a ſolution of opium is injected in the ſame manner.

The frog, I had found from another experiment, is affected preciſely in this way when the cranium is perforated, and the ſolution immediately applied to the brain.

After ſecuring the aorta in other four frogs, a few drops of the ſame ſolution were injected into the heart, through a hole made in the auricle. It was inſtantly deprived of motion; but, with an exception I am about to take notice of, the other ſymptoms, obſerved in the laſt experiment, did not ſupervene.

No trembling nor ſpaſmodic contractions of the muſcles took place; the frogs continued to move their fore-limbs and eyes, as long, and, in ſhort, died in preciſely the ſame way, as frogs do that die in conſequence of the heart being cut out. In one of them, which was very large, the eyes moved when irritated for about two hours.

In the firſt frog uſed in this experiment, a circumſtance occurred, which at firſt appeared quite unaccountable.

Its eyes gradually loſt their ſenſibility, till, in the ſpace of about ten minutes, they could not by any irritation be excited to motion. This, however, they gradually recovered and preſerved, as has been mentioned. While the eyes were thus affected, the fore-limbs alſo were to a conſiderable degree deprived of motion, which they too recovered.

Theſe ſymptoms I could only attribute to a little of the ſolution remaining on my fingers, and the inſtrument employed in opening the thorax, which might have been conveyed to the maſs of blood, and through this medium applied to the brain, before the aorta was ſecured. That this conjecture was juſt, appears from what happened to the other three frogs uſed in this experiment.

Having repeatedly waſhed my hands and the inſtrument with cold water, before I handled the next frog, very little of this affection was obſerved in it; and as it was allowed to lie about ten minutes after ſecuring the aorta, the affection was at its height before the ſolution was injected into the heart, by which it was not in the leaſt increaſed. It gradually went off, as in the former caſe.

Before touching the third frog uſed in this experiment, I waſhed my hands and the inſtrument with warm water and ſoap, which entirely prevented any affection, either of the eyes or fore-limbs, in it. Neither did this occur in the laſt frog on which the experiment was made, when I had not been previouſly handling the ſolution.

I take notice of theſe circumſtances, becauſe they not only ſhew, how ſmall a quantity of tobacco is capable of affecting this animal, and how readily it is received into the maſs of blood, but alſo ſuggeſt a neceſſary precaution in making ſuch experiments.

The ſtate of the muſcles after death was not examined in the firſt frog uſed in theſe experiments; in the other ſeven, they contracted readily, on wounding the nerves which terminate in them, except in one, which was very young, and which had lain dead a conſiderable time before the ſtate of its muſcles was examined.

Leſt it ſhould be ſaid, that interrupting the circulation in the latter experiment prevented the tobacco producing the effects obſerved in the former, the following was made.

After ſecuring the aorta by ligature, and permitting the blood to eſcape, by wounding the auricle in three frogs, and cutting out the heart of a fourth, the cranium of each was perforated, and as much of the ſolution as poſſible applied to the brain.

They were all immediately ſeized with the moſt violent trembling; their fore-limbs became paralytic, and their eyes fixed preciſely as happened when the ſolution of tobacco was thrown into the heart, without previouſly ſecuring the aorta. Their limbs contracted readily after death, on ſtimulating the nerves that go to them.

When a tube, containing a ſolution of tobacco, is forced along the ſpinal marrow, the hinder-limbs are inſtantly rendered paralytic, as the fore ones are when the ſolution is applied to that part of the brain which is lodged within the cranium; for ſome of Dr. Monro's obſervations, as well as this experiment *, prove, that at leaſt part of that portion of the brain which ſupplies the hinder-limbs in the frog, is lodged in the ſpine.

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* This experiment, compared with the following, alſo proves another circumſtance, that a much larger proportion of tobacco, when it is received into the ſyſtem by means of the abſorbents, is ſent to the brain, than to the ſpinal marrow. This indeed we might, *a priori*, have expected from the great quantity of blood ſent to the former.

The following experiment was made, to ſhew the comparative effects of tobacco, applied to the inteſtines of the entire frog, and to thoſe of the ſame animal with the heart cut out; where it can only act through the medium of the nerves of the part to which it is directly applied.

The firſt pair of frogs on which the experiment was made, were young, and very nearly of the ſame ſize: they were equally vigorous. Into the inteſtines of the larger, without removing the heart, twenty-eight drops of the ſolution were injected, the greater part of which was returned.

This frog was not examined till forty-two minutes after the injection of the ſolution; it was then found without any ſign of life, except that, on ſuddenly letting fall the hinder-limbs, they were ſeized with a trembling motion, which laſted a few ſeconds. No motion could be excited in the eyes, and the fore-limbs were quite paralytic.

The heart of the other frog was removed, and twenty-two drops of the ſame ſolution injected into the inteſtines, very little of which was returned. This frog was affected with no trembling. It moved its eyes, when they were irritated, ſeventy-three minutes after the injection of the ſolution, and retained the motion of the fore-limbs, as long as that of the hinder ones.

On irritating the nerves after death, the muſcles contracted readily in both theſe frogs. More of the ſolution was found in the latter than in the former.

The ſecond pair were alſo young: they were of the ſame ſize, and equally vigorous.

Into the inteſtines of the firſt, without removing the heart, twenty-three drops of the ſame ſolution were injected; the half at leaſt was returned. Twenty-two minutes after the injection of the ſolution, this frog was found in exactly the ſame ſituation in which the firſt of the laſt pair was found at the expiration of forty-two minutes. After removing the heart of the other, twenty-three drops were thrown into its inteſtines; fifty-eight minutes after the ſolution was injected, it moved its eyes when they were irritated. It died in the ſame manner as the ſecond of the former pair. The irritability of the muſcles in both remained after death.

Third pair. The reſult of this experiment in all reſpects reſembled that of the laſt.

The fourth pair were full grown, and equal in ſize and vigour. The reſult of this experiment was again ſimilar to that of the foregoing. The entire frog ſoon became affected with violent trembling. Fourteen minutes after the injection of the ſolution, no motion could be excited in the eyes, and the fore-limbs were paralytic. The other died as the ſecond of the other pairs did. It moved its eyes eighty-nine minutes after the ſolution was injected.

As a large quantity (50 drops) was thrown into each of theſe frogs, the inteſtine gave way; ſo that the ſolution got into the cavity of the abdomen; and in the latter, part of it eſcaped by the opening at which the heart was extracted. Contractions were readily excited in the muſcles of both after death.

The fifth pair were likewiſe full grown, and both uncommonly large. The one whoſe heart was cut out was rather ſmaller than the other. They were equally vigorous. Sixty-four drops of the ſolution were injected into the inteſtines of each of them; which in this caſe alſo were ruptured in both frogs. None of the ſolution, however, was returned by the opening made for extracting the heart. In ſix minutes the fore-limbs of the entire frog were paralytic, and no motion could be excited by irritating its eyes; the hinder-limbs were affected with very violent trembling, and at times with ſtrong ſpaſms, reſembling thoſe induced by opium. I have obſerved this in a leſs degree in other inſtances, when tobacco was thrown into the inteſtines of the entire frog. The muſcles of the hinder-limbs of this frog were found, after death, almoſt quite void of irritability.

As for the other, it retained all its motions for fifty-tree minutes after the ſolution was injected; thoſe of the fore-limbs as perfectly as thoſe of the hinder ones: its eyes moved, when irritated, nineteen minutes longer; and its muſcles contracted after death with unuſual force.

All the frogs uſed in this experiment became languid ſoon after the injection of the ſolution. In eight or ten minutes, however, they were conſiderably leſs ſo; preciſely as happened in a ſimilar experiment made with opium.

Whether the heart be previouſly removed or not, ſlight convulſive twitchings (chiefly on the back) are ſometimes obſerved immediately after injecting a ſtrong ſolution of tobacco into the ſtomach and inteſtines, or cavity of the abdomen, of a frog, reſembling thoſe which often take place in the human body, when a violent topical irritation is preſent. They are only to be perceived for a minute or two after the injection of the ſolution.

From the foregoing experiments with

tobacco, then, it appears, that the ſymptoms which it produces, when thrown into the heart, are the ſame with thoſe excited by its immediate application to the brain: that theſe ſymptoms, when the tobacco is exhibited in the former way, proceed from no action of the tobacco on the nerves of the heart, but from its being conveyed through the aorta, and immediately applied to the brain; ſince they do not follow its injection into the heart, when the aorta is previouſly ſecured by ligature, although it was found, that interrupting the circulation does not unfit the nervous ſyſtem from undergoing the change neceſſary for the production of ſuch ſymptoms. It alſo appears from theſe experiments, that tobacco produces the ſame effects, though more ſlowly, when thrown into the ſtomach and inteſtines, as when thrown into the heart; that in the former caſe, as in the latter, they are ſtill to be aſcribed to the tobacco being received into the ſanguiferous ſyſtem, and immediately applied to the brain; and that the effects of this drug, when it acts merely on the nerves of the part to which it is applied, do not eſſentially differ from thoſe of any ſtrong topical irritation. It may alſo be collected from theſe experiments, that the preſence of tobacco in the ſyſtem, like that of opium, only affects the irritability of the muſcles of voluntary motion, when it produces convulſions in them; *i. e.* when it is applied in conſiderable quantity to the brain. It appears, therefore, that the modus operandi of tobacco on the living animal body is in every inſtance analogous to that of opium.

May not poiſons, in general, be divided into two claſſes: The firſt comprehending thoſe which, applied to the ſentient extremities of the nerves, produce effects on the ſyſtem in general, not eſſentially different from the effects of mechanical irritation; but which ſeem incapable of any other action through the medium of the nerves, although applied to them after laceration; their effects on the ſyſtem, when infuſed into a wound, differing only in degree from thoſe produced by injecting them into any of the cavities of the body; ſuch are opium, tobacco, and a great variety of other poiſonous drugs: The ſecond claſs comprehending the poiſons which ſeem leſs apt to affect the ſentient extremities of the nerves in the ſound ſtate, but, applied to lacerated nerves, produce through them effects eſſentially different from thoſe of mere topical irritation; ſuch are the poiſon of the viper, that of rabit animals, and ſome others?

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